Office Action Summary	Application No.	Applicant(s)	
	09/534,825	FRUDAKIS ET AL.	
	Examiner	Art Unit	
	Alana M. Harris, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 June 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-16 and 21-69* is/are pending in the application.

4a) Of the above claim(s) *4-16 and 21-60* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *61-69* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *15* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Response to Arguments

1. Claims 4-16 and 21-69 are pending.

Claims 4-16 and 21-60, drawn to non-elected inventions are withdrawn from examination.

Claims 61-69 have been added.

Claims 1-3 and 17-20 have been cancelled.

Claims 61-69 are examined on the merits.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Information Disclosure Statement

3. The information disclosure statement filed October 23, 2000, Paper No. 7 lists a number of documents that were to be considered by the Examiner. Applicants submitted the documents that were "lined through" by the Examiner and supplied with the first action on the merits. All of the documents listed on the IDS have been reviewed and considered.

Withdrawn Objections

Claim Objections

4. Claims 1-3, 17 and 18 are no longer objected to because they have been cancelled.

Withdrawn Rejections

Claim Rejections - 35 USC § 112

5. The rejection of claims 1 and 2 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is withdrawn in light of the cancellation of the claims.

6. The rejection of claims 17-20 under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement commensurate with the scope of the claimed invention is withdrawn in light of the cancellation of the claims.

7. The rejection of claims 1 and 2 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of the cancellation of the claims.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

8. Claims 62 and 63 are rejected under 35 U.S.C. 112, first paragraph, because the specification, does not reasonably provide enablement commensurate with the scope of the claimed invention. The specification does not enable any person skilled in the art to

which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Claim 62 is broadly drawn to "[a]n isolated polypeptide that is at least 90% identical to the amino acid sequence of SEQ ID NO:299" and claim 63 is drawn to an isolated polypeptide 95% identical to the said sequence. The specification while being enabling for the polypeptide having the amino acid sequence of SEQ ID NO:299, does not reasonably provide enablement for variants that have at least 90% or 95% sequence identity. There is no guidance as to how to make these divergent sequences. The products of these 90% and 95% sequence identical molecules may possess function that is not commensurate with the functions of the native protein. The 90% and 95% sequence identical amino acids may not maintain the activities proposed in the specification. It would seem that specific function(s) would be required to make the encoded protein useful for the applications disclosed in the specification, such as pharmaceutical compositions. Since the amino acid sequence of a polypeptide determines its structural and functional properties, predictability of which changes can be tolerated in a polypeptide's amino acid sequence and still retain similar activity requires a knowledge of and guidance with regard to which amino acid or acids in the polypeptide's sequence, if any, are tolerant of modification and which are conserved and detailed knowledge of the ways in which the protein's structure relates to its function. The specification provides essentially no guidance as to which of the infinite possible choices is likely to be successful. The true fact of the state of the art in peptide chemistry is expressed succinctly in the accompanying Lazar article (Molecular and

Cellular Biology 8(3): 1247-1252, March 1988). This article presents data that substantiates the fact that the introduction of mutations in an amino acid sequence will yield products with different biological activity from the wild type protein.

From the discussion above, it is clear that the predictability of changes to the amino acid sequence is practically nil as far as biological activities are concerned. The specification fails to provide sufficient guidance to enable one of ordinary skill in the art to make and use the claimed nucleic acids in a manner reasonably correlated with the broad scope of the claims. Without such guidance, the changes which must be made in the nucleic acid sequence of SEQ ID NO: 292, which results in amino acid sequences with at least 90% identity is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue.

9. Claims 61-69 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 61 is broadly is drawn to a polypeptide comprising SEQ ID NO: 299, wherein said polypeptide is expressed in breast tumor protein. Claims 62 and 63 are broadly drawn to 90% and 95% identical to the amino acid sequence of SEQ ID NO: 299, respectively. The balance of the claims are drawn to the said sequence encoded by polynucleotide sequence, SEQ ID NO: 292 and the encoded product, SEQ ID NO: 299 in combination with a carrier and an immunostimulants. The specification alleges

that the claimed polypeptides can be used in compositions for the diagnosis and methods for the diagnosis, monitoring and therapy of breast, see page 8, lines 6-14. The specification does not evidence enabling disclosure providing that the claimed breast tumor protein can be used for the immunotherapy of breast cancer as suggested, see bridging paragraph of pages 23 and 24. The specification has not presented evidence of the use of a breast tumor protein. There is a dearth of extensive chemical characterization of the structure of this breast tumor protein. This is in fact necessitated in order to elucidate its effectiveness as immunotherapeutic capable of establishing an immunogenic response.

The specification suggests the use of immunogenic portions of the breast tumor in compositions that would establish an immunogenic response, however clinically successful specific cancer immunotherapy depends on the identification of the immunogenic portions or tumor-rejection antigens. Applicants have not presented objective evidence that supports the use of the claimed polypeptides in assays, for example that analyze either T-cell or antibody responses of cancer patients against autologous cancer cells. It is not clear that Applicants' breast tumor protein would even generate a modest immune response or how to generate relatively potent immune responses. Furthermore, SEQ ID NO: 299 is referred to as a breast tumor-specific polypeptide, however it is reasonable to doubt its specificity based upon an identical sequence listed in U.S. Patent 6,329,505 (December 11, 2001). This patent and the attached database sheet evidence that a sequence identical to Applicants' SEQ ID NO: 299 is useful in compositions and methods for the diagnosis and therapy of prostate

cancer, see columns 1 and 2 of patent '505. Hence, there is lack of instruction in the specification enabling one skilled in the art to make and practice the invention commensurate within its suggested applications within the specification utilizing the broadly claimed breast tumor proteins. The specification provides insufficient guidance with regard to these issues and provides no working examples which would provide guidance to one skilled in the art. For the above reasons, it appears that undue experimentation would be required to use the claimed invention.

Conclusion

10. Claims 61-69 are free of the art.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (703) 306-5880. The examiner can normally be reached on 6:30 am to 4:00 pm, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached on (703) 308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4315 for regular communications and (703) 308-4315 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Alana M. Harris, Ph.D.
August 12, 2002

Sheela Huff
SHEELA HUFF
PRIMARY EXAMINER